B6 Cont.

41. The foam enema according to Claim 28, wherein the xanthan gum is present in an amount of about 400 to 2000 mg per unit dose.- -

REMARKS

Claims 1-4, 6, and 8-15 and 22-41 remain pending after amendment.

Specification Amendments

The paragraph bridging pages 7 and 8 of the specification is amended to recite the range of claim 13. No new matter is added by this amendment.

Claim Amendments

By this amendment, claims 5 and 7 are cancelled. The limitations of claim 5 are added to claims 1-4 and 6. New claims 29-41 are added. No new matter is added by this amendment.

Rejection under 35 USC 112 (paragraph one)

Claims 1, 9, 11, 13, 14 and 27 stand rejected under 35 USC 112 (paragraph one). This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

In response, claim 1 is amended to delete reference to "rectal administration".

Contrary to the position of the Examiner, the range recited in claims 9 and 27 is supported at page 8, line 7 of the specification. The range recited in claim 11 is supported at page 9, line 13 of the specification. The specification is amended at page 7 to provide basis for the range of claim 13. The range in claim 14 is supported at page 9, lines 8-9 of the specification.

The rejection is thus without basis and should be withdrawn.

Rejection under 35 USC 112 (paragraph one)

Claim 1 stands rejected under 35 USC 112 (paragraph two) as not distinctly claiming the invention. This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

In response, claim 1 is amended to correct the improper Markush language. The rejection is accordingly without basis and should be withdrawn.

Rejection under 35 USC 102(b) over Day

Claims 1, 2, 9 and 27-28 stand rejected under 35 USC 102(b) as being anticipated by Day WO 94/04136. This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

In response, applicants note that the cited reference discloses the use of an anion-binding polymer with a hydrophilic polymer to treat IBS. The reference is silent with

respect to the treatment of IBD and, on this basis, it would appear that the Examiner fails to appreciate the difference between IBS and IBD. IBS (irritable bowel syndrome) is distinguished from IBD (inflammatory bowel disease) in that there is chronic inflammation of the mucosa and sub-mucosa layers of the intestine in IBD. By contrast, IBS involves abnormally increased motility of the small and large intestines without any detectable radiological or histological evidence of organic pathology, such as observable inflammation of layers deeper than the epithelium. Effective treatment of IBS is not necessarily an effective treatment of IBD.

While the anion-binding polymer and hydrophilic polymer can be administered separately, the reference states at page 11, lines 12-15 that:

> "It is only the combination of the anion-binding polymer and hydrophilic polymer which is effective in preventing and relieving symptoms of this disease."

The anion-binding polymer is present as a bile acid sequestrant (see page 10, lines 14-17), but there is no indication that, as a class, the hydrophilic polymer has any function other than for its hydrophilic activity. Exemplified hydrohilic polymers include xanthan gum, but the reference fails to suggest that the gum has any pharmacological effect on either IBD or IBS.

The reference also fails to exemplify the use of xanthan gum, and is also silent with respect to the use of HPMC. Moreover, the reference discloses only

an oral method of administration, with the reference being silent with respect to coating or any other method of providing a delayed release oral formulation.

As discussed above, the reference contains no teaching or suggest of the therapeutic use of xanthan gum or HPMC in the treatment of IBD (either by oral or rectal administration). The reference also fails to disclose or suggest the use of xanthan gum in an amount of from about 0.4 to 2.0 wt. % in such a pharmaceutical composition suitable for rectal treatment of IBD.

The rejection is accordingly without basis and should be withdrawn.

Rejection under 35 USC 102(b) over Astra

Claims 1, 3-5, 7, 8, 11, 12, 14-15 and 22-26 stand rejected under 35 USC 102(b) as being anticipated by Astra WO 98/01112. This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

In response, applicants note that the reference published on January 15, 1998, which date is subsequent to the priority date of June 19, 1997 for the above application. The Astra publication thus does not constitute prior art against the claimed invention.

Rejection under 35 USC 102(b) over Slagel

Claims 1, 10 and 13 stand rejected under 35 USC 102(b) as being anticipated by Slagel WO 96/03115. This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

In response, applicants note that the cited reference relates to bag-in-can and can-in-can foam enemas. The bag or can contains an aqueous foamable composition having a delayed foaming action and containing a water-soluble polymer exemplified by, for example, HPMC and xanthan gum (see page 6, lines 1-4). However, the reference teaches that:

> "The precise identity of the water-soluble polymer in the compositions of the invention is not critical . . ." (see page 5, lines 33-34).

The reference makes reference to the treatment of both IBD and IBS at page 6, lines 34-35. The foamable composition of Examples 1-5, 9-11, 15-17, 22-27 and 30 all contain xanthan gum but are silent with respect to the use of HPMC in the exemplified compositions.

Further, the reference fails to disclose or suggest the use of xanthan gum in an amount of from about 0.4 to 2.0 wt. % in such a pharmaceutical composition suitable for rectal treatment of IBD.

The rejection is thus without basis and should be withdrawn.

Rejection under 35 USC 102(b) over Sandborn

Claims 1 and 6 stand rejected under 35 USC 102(b) as being anticipated by Sandborn WO 96/30021. This rejection respectfully is traversed to the extent deemed to apply to the claims as amended.

The reference discloses the treatment of IBD by topical administration to the colon of azathioprine. Reference is made to both oral and rectal administration (see page 1, lines 29-33). The oral dosage form can be enterically coated to delay release to the terminal ileum and/or colon. The reference makes general reference to the use of gums and modified celluloses as carriers in enema formulations (see page 4, lines 1-3). The foam enemas of Examples 1 and 2 contain xanthan gum as a suspending agent in a concentration of about 0.2 wt. %.

As discussed above, the reference contains no teaching or suggest of the therapeutic use of xanthan gum or HPMC in the treatment of IBD (either by oral or rectal administration). The reference also fails to disclose or suggest the use of xanthan gum in an amount of from about 0.4 to 2.0 wt. % in such a pharmaceutical composition suitable for rectal treatment of IBD.

The rejection is thus without basis and should be withdrawn.

The application is now believed to be in condition for allowance and an early indication of same is earnestly solicited.

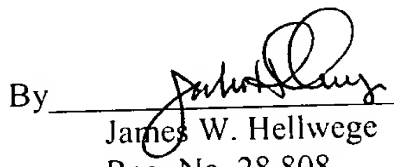
In the event that any outstanding matters remain in this application, Applicants request that the Examiner contact James W. Hellwege (Reg. No. 28,808) at (703) 205-8000 to discuss such matters.

Applicant respectfully petitions under the provisions of 37 CFR 1.136(a) and 1.17 for a three-month extension of time in which to respond to the Examiner's Official Action. The Extension of Time fee in the amount of $920.00 is attached hereto.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Very truly yours,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By 

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SPECIFICATION AMENDMENTS WITH MARKINGS TO SHOW CHANGES

Replace the paragraph beginning at page 7, line 36 and continuing to line 16 of page 8 with the following new paragraph:

- - A suitable dosage for xanthan gum in an enema or foam enema is 200 to 2000 mg, preferably 250 or 400 to 2000 mg, more preferably 250 to 1650 mg, more preferably still 400 to 1650 mg, especially 550 to 1000 mg, in an aqueous or non-aqueous carrier. The volume of a liquid enema is typically 50 to 200 cm^3 , preferably about 100 cm^3. A suitable % w/w of xanthan gum in an enema is (based on 100 cm^3 enema) 0.2% to 2% w/w, more preferably 0.3% to 2% w/w, more preferably still 0.4 to 2% w/w, more preferably still up to 1.65% w/w, and still more preferably 0.55% to 1%. Suitably the volume of a foam enema is 20 to 40 cm^3. Based on the above preferred dosages, a suitable % w/w of xanthan gum in a foam enema (based on 40 cm^3 foam enema) is 1% to 4.25% w/w, more preferably 1.4% to 2.5%. A buffer is preferably added to the liquid or foam enema of xanthan gum to stabilize the pH. When a buffer is used it increases the viscosity and as a result, the maximum % w/w of xanthan gum that can be incorporated in the enema is about 1.7 % w/w. - -

CLAIM AMENDMENTS WITH MARKINGS TO SHOW CHANGES

Please cancel claims 5 and 7 without prejudice or disclaimer of the subject matter therein.

Amend the claims as follows:

1. (Twice Amended) A [rectally administrable or] post-gastrically available delayed release oral (DRO) pharmaceutical composition for the treatment or prophylaxis of inflammatory bowel disease (IBD), said composition comprising a polysaccharide selected from the group consisting of xanthan gum and hydroxypropylmethylcellulose (HPMC) as a therapeutically active agent in an amount effective to treat inflammatory bowel disease, together with a pharmaceutically acceptable carrier or vehicle.

2. (Twice Amended) The DRO pharmaceutical composition according to Claim 1, wherein the polysaccharide is xanthan gum.

3. (Twice Amended) The DRO pharmaceutical composition according to Claim 1, wherein the polysaccharide is HPMC

4. (Twice Amended) The DRO pharmaceutical composition according to Claim 1, wherein the polysaccharide is present as the sole therapeutically active ingredient.

6. (Twice Amended) The DRO pharmaceutical composition according to Claim [5 which DRO] 1, said composition [is]being an enteric coated dosage form adapted to release its contents within the region of the jejunum to the colon.

8. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [7] 29 which is a liquid enema or foam enema.

9. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [2] 30, which is a liquid enema containing xanthan gum in a concentration of about 0.4 to about 2 % w/w (based on the composition).

10. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [2] 30, which is a foam enema containing xanthan gum in a concentration of about 1.4 to about 2.5 % w/w (based on the composition).

11. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [3] 32, which is a liquid enema containing HPMC in a concentration of about 1 to about 20 % w/w (based on the composition).

12. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [3] 32, which is a foam enema containing HPMC in a concentration of about 2.5 to about 25 % w/w (based on the composition).

13. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [7] 29, wherein the polysaccharide is xanthan gum in an amount of about 400 to about 2000 mg per unit dose.

14. (Twice Amended) The rectally administrable pharmaceutical composition according to Claim [7] 29, wherein the polysaccharide is HPMC in an amount of about 1 to about 20 g per unit dose.

15. (Twice Amended) The DRO pharmaceutical composition according to Claim [5] 1 in unit dose form containing about 400 to about 2000 mg of the polysaccharide per unit dose.

22. (Twice Amended) A method for the treatment or prophylaxis of inflammatory bowel disease (IBD) comprising contacting the diseased mucosa of the gastro-intestinal tract with a therapeutic amount of a polysaccharide selected from the group consisting of xanthan gum and hydroxypropylmethyl-cellulose (HPMC).